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Docket No. 289603US0PCT
IN RE APPLICATION OF: Kohei YAMADA, et al.
SERIAL NO: 10/577,064
FILED: April 24, 2006
FOR: ALPHA-1-PHOSPHORYLATED-2-DEOXY-2-FLUOROARABINOSIDE AND PROCESS FOR PRODUCING 2'-DEOXY-2'-FLUORO-BETA-D-ARABINONUCLEOSIDE

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

SIR:
Transmitted herewith is an amendment in the above-identified application.

■ No additional fee is required

☐ Small entity status of this application under 37 C.F.R. §1.9 and §1.27 is claimed.

■ Additional documents filed herewith: Preliminary Amendment

The Fee has been calculated as shown below:

CLAIMS	CLAIMS REMAINING		HIGHEST NUMBER PREVIOUSLY PAID	NO. EXTRA CLAIMS	RATE	CALCULATIONS
TOTAL	16	MINUS	20	0	x $50 =	$0.00
INDEPENDENT	6	MINUS	6	0	x $200 =	$0.00
		☐ MULTIPLE DEPENDENT CLAIMS			+ $360 =	$0.00
		TOTAL OF ABOVE CALCULATIONS				$0.00
		☐ Reduction by 50% for filing by Small Entity				$0.00
		TOTAL				$0.00

☐ A check in the amount of **$0.00** is attached.

☐ Credit card payment form is attached to cover the fees in the amount of **$0.00**

■ Please charge any additional Fees for the papers being filed herewith and for which no check or credit card payment is enclosed herewith, or credit any overpayment to deposit Account No. 15-0030. A duplicate copy of this sheet is enclosed.

■ If these papers are not considered timely filed by the Patent and Trademark Office, then a petition is hereby made under 37 C.F.R. §1.136, and any additional fees required under 37 C.F.R. §1.136 for any necessary extension of time may be charged to Deposit Account No. 15-0030. A duplicate copy of this sheet is enclosed.

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DOCKET NO: 289603US0PCT

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF :

KOHEI YAMADA, ET AL. : ATTN: APPLICATION DIVISION

SERIAL NO: 10/577,064 :

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FOR: ALPHA-1-PHOSPHORYLATED-2-DEOXY-2-FLUOROARABINOSIDE AND PROCESS FOR PRODUCING 2'-DEOXY-2'-FLUORO-BETA-D-ARABINONUCLEOSIDE :

PRELIMINARY AMENDMENT

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

SIR:

Please amend three paragraphs of this application. The paragraphs to be amended are [0009] starting on page 4, [0088] on page 25, and [0096] starting on page 28. The amendments are shown in the following paragraphs:

Means for Solving the Problems

[0009]

In view of the foregoing, the present inventors have conducted extensive studies, and as a result have found that (i) 1-phosphorylated-2-deoxy-2-fluoroarabinoside is unexpectedly stable in an aqueous solution, and the a-isomer of the fluoroarabinoside is fully available as a substrate for nucleoside phosphorylase; (ii) α-l-phosphorylated-2-deoxy-2-fluoroarabinoside is stereoselectively produced through hydrolysis and phosphorylation of a 2-deoxy-2-fluoroarabinose derivative represented by formula (III); (iii) phosphorylation of a compound

represented by formula (III) in the presence of a strong ~~base~~ acid salt produces a mixture of α- and β-isomers of 1-phosphorylated-2-deoxy-2-fluoroarabinoside, in which the proportion of the α-isomer, which serves as a substrate for nucleoside phosphorylase, is higher than that of β-1-phosphorylated-2-deoxy-2-fluoroarabinoside, which does not serve as a substrate for the enzyme; and (iv) 2'-deoxy-2'-fluoro-β-D-arabinonucleoside is produced at high yield without employment of two types of nucleoside phosphorylases, when the raw material to be employed is 1-phosphorylated-2-deoxy-2-fluoroarabinoside (α-isomer or a mixture of α- and (β-isomers) instead of 2'-deoxy-2'-fluoro-β-D-arabinopyrimidinenucleoside. The present invention has been accomplished on the basis of these findings.

[0088]

Examples of the aryloxy group include those having any of the aforementioned aryl groups. Specific examples include a phenoxy group; alkylphenoxy groups having any of the aforementioned Cl-C6 alkyl groups, such as methylphenoxy and ethylphenoxy; alkoxyphenoxy groups having any of the aforementioned Cl-C6 alkoxy groups, such as methoxyphenoxy and ethoxyphenoxy; alkylaminophenoxy groups having any of the aforementioned Cl-C6 alkylamino groups, such as dimethylaminophenoxy and diethylaminophenoxy; and halogenophenoxy groups having any of the aforementioned halogen atoms, such as ~~chlorophenyl~~ chlorophenyloxy and ~~bromophenyl~~ bromophenyloxy.

[0096]

The compound (VII) can also be produced by adding a nucleoside phosphorylase and a nucleosidase to the compound (I) or the $\alpha\beta$-isomers mixture (V') and to a guanosine 5'-monophosphate. The reaction can be performed through addition of the nucleoside phosphorylase and nucleosidase (about 5 units/mL or more each) in a buffer solution such as a Tris-HCl buffer solution or a phosphate buffer solution at 20 to 70°C for about 1 to about 100 hours with, if desired, stirring.